have OH at any position which in turn can be etherified or esterified, keto groups, amino groups or halogens (see definition of Q in claim 1).

These comments do not relate to the obviousness-type double patenting rejection or applicants' rebuttal of that rejection.

In claim 1 of US '368 and claim 1 of US '791, group Z is defined as H, OH or alkanoyloxy group having 1-9 carbon atoms. Group L is defined as either $-CH_2$-A-B- or -D-CHE-CHF-G-. A is O and B is $-(CH_2)_n$- with n being 1-6. D is a direct bond, a methylene bridge or a 1,2-ethenediyl bridge (i.e., an E-double bond) between carbon atoms 20 and 22; E and F are each hydrogen atom or together form a second bond (E-double bond) bond; and G is a direct bond or is $-(CH_2)_n$- with n being 1-6 and in which a $-CH_2$- group can be replaced by a oxygen atom.

Thus, in the claims of both US '368 and US '791, the structure from the C-20 atom is $-C^{20}R_1R_2$-CH_2-O-$(CH_2)_{1-6}$-CR_3R_3Z or $-C^{20}R_1R_2$-D-CHE-CHF-$(CH_2)_{0-6}$-CR_3R_3Z. On the other hand, in applicants' claim 1 the structure from the C-20 atom is $-C^{20}R_3R_4$-CHV-CHW-Q-cyclopropyl-Z in which Q is not -CHOH-, and in claim 30 it is $-C^{20}R_3R_4$-CHV-CHW-Q-cyclopropyl-Z in which Q is $-CH_2$- or $-CH_2-CH_2$-. In these structures, V and W are an E-double bond or V is OH and W is H. In claim 1, Q is defined as a carbon unit having up to 10 carbon atoms which have can have alpha or beta hydroxy groups, amino groups, and/or halogen atoms and wherein the mentioned hydroxy groups can be esterified or etherified, but is not -CHOH-.

Nothing in the rejection, or the claims of US '368 and US '791, suggests modifying either $-CH_2$-A-B- or -D-CHE-CHF-G- so as to arrive at structure in accordance with that possessed by compounds of applicants' claimed invention. For example, nothing suggests selecting D to be a single bond while CHE-CHF is a double bond and CR_3R_3Z is cyclopropyl-Z. None of the claims require D to be a single bond. Also, none of the claims require CHE-CHF to be a double bond. Conversely, several claims require the compounds to possess the structure $-CH_2$-A-B-, rather than the structure -D-CHE-CHF-G-. See claims 8, 11, 12, and 13 of US '368 and claims 8 and 9 of US '791.

Furthermore, while it is the claims rather than the specification that are relevant in double-patenting rejections, it is noted that the specification does not provide guideposts the lead to a structure in which D is a single bond while CHE-CHF is a double bond and CR_3R_3Z is cyclopropyl-Z. None of the disclosed compounds or subgenera require D to be a single

bond. Also, none of the disclosed compounds or subgenera require CHE-CHF to be a double bond. See the side chains listed in the text bridging columns 1-2 and 3-4. See also the specific compounds listed at columns 3-4 and 6 and in the Examples.

The rejection fails to state any reasons as to why the claimed subject matter is considered to be obvious in view of the claims of US '368 or US '791. In the rejection, it is merely asserted that the instantly claimed subject matter is "fully disclosed in the patent and is covered by the patent." Thereafter, it is stated that the claimed invention "is drawn to the vitamin D derivatives which are considered obvious over the claims of the prior U.S. patent issued to the same inventor and same assignee." **These statements merely present an unsupported conclusion of obviousness.**

With respect to any double patenting rejection, it is the claims in the reference which are to be relied on, not the disclosure in the specification. Nothing within the claims of US '368 and/or US' 791 provides any motivation that would lead one to a compound in accordance with applicants' claim 1 or claim 30. No rationale is presented in the rejection as to why the claimed compounds are considered obvious in view of the **claims** of US '368 and US '791. Moreover, nothing within the rejection speaks to the requisite motivation that would lead one of ordinary skill in the art, based on the claims of US '368 and/or US '791, to a compound in accordance with the claimed invention. For these reasons alone, the obviousness-type double patenting rejection should be withdrawn.

In view of the above remarks, it is respectfully submitted that neither the claims of US '368 nor the claims of US '791 render obvious applicants' claimed invention. Withdrawal of the obviousness-type double patenting rejection is respectfully requested.

Rejection Under 35 U.S.C. §103 In View of Kirsch et al. (WO '242)

Claims 1-3, 5, 6, 8-11, and 14-30 are rejected as being obvious under 35 USC §103 in view of Kirsch et al. This rejection is respectfully traversed.

This rejection is repeated from the Office Action of September 12, 2000. Applicants traversed the rejection in the March 12, 2001 Amendment. This rejection was also repeated in the Office Action of June 4, 2001. Applicants again traversed the rejection in the December 4, 2001 Reply. The only response to Applicants' arguments in the recent Office Action is reproduced above.

Applicants' wish to inform the Examiner that the U.S. National Phase corresponding to WO '242, i.e., Serial No. 08/981,819 (filing date March 31, 1998), issued as US 6,372,731

on April 16, 2002. A continuation application of Serial No. '819, i.e., Serial No. 09/738,286 which was filed on December 18, 2000, issued as US 6,376,480 on April 23, 2002. Copies of US '731 and US '480 are enclosed for the Examiner's convenience.

In the rejection, reference is made to formula I at page 1 and Example XXXIV at page 36. Further, it is argued that WO '242 discloses 3-7 numbered carbocyclic or heterocyclic ring groups at the C-25 position.

In formula I of WO '242, the C-24 position is substituted by Groups A and B. Groups A and B can together form a keto group. Alternatively, Group A can be OR' and B can be a hydrogen atom or B can be OR' and A can be a hydrogen atom. R' is a hydrogen atom, an alkanoyl group of up to 9 carbon atoms, or an aroyl group. Thus, in formula I of WO '242, the structure from the C-20 position is $-C^{20}R_3R_4$-CH=CH-CO-$C^{25}R_5R_6Z$ or $-C^{20}R_3R_4$-CH=CH-CHOR'-$C^{25}R_5R_6Z$. The structure(s) form by R_5 and R_6 are broader than 3-7 numbered carbocyclic ring groups mentioned in the rejection. These groups can each be H. Cl, F, trifluoromethyl, or straight-chain or branched chain, saturated or unsaturated hydrocarbon radicals with up to 4 carbon atoms, in addition to forming 3-7 membered, saturated or unsaturated carbocyclic groups with the carbon atom at the 25 position.

On the other hand, as noted above, in applicants' claim 1 the structure from the C-20 atom is $-C^{20}R_3R_4$-CHV-CHW-Q-cyclopropyl-Z in which Q is not -CHOH- and in claim 30 it is $-C^{20}R_3R_4$-CHV-CHW-Q-cyclopropyl-Z in which Q is $-CH_2-$ or $-CH_2-CH_2-$.

The Examiner argues that WO '242 is generic to the claimed invention. However, there is no rationale presented in the rejection as to what motivation would lead one a compound in accordance with the applicants' claimed genus, either by selection or modification. Furthermore, the rejection does not address applicants' claims that are even further distinguished from the disclosure of WO '242. See, e.g., claims 2, 3, 19, 23, 24, and 27.

Aside from formula I, the only compound cited in the rejection is the compound of Example XXXIV. The compound of formula XXXIV at page 36 exhibits a cyclopropyl group at the C-25 position and at the C-24 position exhibits the group $CHOR_{11}$. In addition, Group Z' is attached to the C-25 position. R_{11} is an acid-labile protective group having a definition analogous to Y'_1 or Y'_2, or is tetrahydropyranyl, tetrahydrofuranyl, ethoxyethyl, methoxymethyl, or methoxyethoxymethyl. See the disclosure at the middle of page 27. Y'_1 is a hydrogen atom or a protected hydroxy group and Y'_2 is a hydroxy protective group. The protective groups are said to preferably be alkyl-, aryl-, or mixed alkylaryl-substituted silyl

groups. Examples of protective groups disclosed by WO '242 are TMS, TES, TBDMA, TBDPS, and TIPS. See the description of Y'_1 and Y'_2 at page 22 immediately following formula II. Z' is analogous to group Z of WO '242 or optionally exhibits protective group-carrying substituents. See the bottom of page 22.

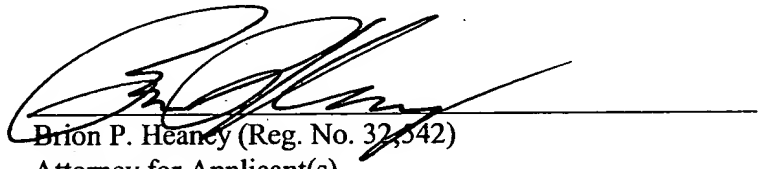
One of ordinary skill in the art presented with the disclosure of WO '242 and its broad genus of compound is not provided with sufficient motivation to modify the compounds disclosed therein in such a manner as to arrive at a compound in accordance with applicants' claims genus. The mere disclosure of a broad genus of compounds does not, in and of itself, establish obviousness with respect to each and every compound encompassed therein. See, for example, *In re Jones*, 21 USPQ 2d 1941 (Fed. Cir. 1991) and *In re Baird*, 29 USPQ 2d 1550 (Fed. Cir. 1994). Instead, the disclosure must provide some motivation which would lead one of ordinary skill in the art, without the benefit of hindsight, to modify the disclosed compounds in such a manner as to arrive at the claimed compound.

In this case, no such motivation is presented in WO '242 or is asserted in the rejection that would lead one of ordinary skill in the art to modify the C-25 cyclopropyl compounds disclosed in WO '242 in such a manner as to arrive at a compound in accordance with applicants' claimed genus. Merely asserting that a reference has a generic disclosure which overlaps a claim does not satisfy the requisite showing of motivation for obviousness as discussed by the Court in *Jones* and *Baird.*

This is particularly the case for the compound of formula XXXIV which is described in WO '242 as an **intermediate** within a synthesis process. There is no motivation to interrupt the synthesis process, isolate the intermediate, and modify its structure. See, e.g., *In re Lalu et al.*, 223 USPQ 1257 (Fed. Cir. 1984).

In view of the above remarks, it is respectfully submitted that Kirsch et al. (WO '242) fails to provide sufficient motivation to render obvious applicants' claimed invention. Withdrawal the rejection under 35 U.S.C. §103 is respectfully requested.

Respectfully submitted,



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